

## REMARKS

This Amendment to the patent application is made in response to an Office Action dated August 12, 2003 in the file of this patent application. Reconsideration of the merits of this application, including the changes made herein, is respectfully requested. Although the Office Action was the first action on the merits since the last filing of a Request for Continued Examination, another RCE is filed herewith to ensure that this submission is properly considered.

Enclosed with this amendment is a Declaration under 35 C.F.R. §1.132 by Tenneille Ludwig. Ms. Ludwig is a Research Associate in the laboratory of Prof. James Thomson, the inventor of this patent application. Ms. Ludwig's declaration is presented to answer a question implied by the last Office Action. The Examiner accepted that there was an unexpected result in the combination of the use of bFGF and the serum replacement in the culture of primate embryonic stem cells. The Examiner noted that the examples used bFGF combined with a specific product, Knockout Serum Replacer, and the Examiner asserted that the claims were broader than this combination. The implied question is therefore whether the unexpected effect is unique to the Knockout Serum Replacer product or is generic to similar media additives. The Ludwig Declaration is intended to present scientific evidence that, as predicted in the present patent application, the effect observed by the applicant here is not limited to the specific Knockout Serum Replacer product, but extends to formulations having the same constituents. Thus, Ms. Ludwig performed experiments to substitute for the Knockout Serum Replacer product with a home-made mixture including essentially the same important constituents. As recited in the declaration, the "TeSR" (or Tenneille Serum Replacer), when used in cultures to grow both human and primate embryonic stem cells gave results comparable to those stem cell cultures grown using the commercial Knockout Serum Replacer product. There was "no significant difference" between the two culture conditions (Ludwig declaration paragraph 10).

The TeSR medium used by Ms. Ludwig included albumin, vitamins, minerals, antioxidants, insulin, transferrin, and lipids (Declaration par. 3). All of these elements have been added to the claims of the application except antioxidants and lipids. The use of antioxidants is obviously for stability, but there is no reason to believe that they are necessary for efficacy. Similarly the use of lipids is helpful, but not believed essential. Thus, all of the recited constituents reasonably believed to be important to the creation of a medium that interacts with the FGF to achieve the unexpected effect are recited now in the claims.

The new constituents recited in the claims find express support in the specification at page 2 in the paragraph beginning at line 25.

As the applicant understands the logic of the Examiner, it has been accepted that the applicant has demonstrated an expected effect, and the Examiner has accepted that the effect can be achieved with other forms of FGF. The Examiner nevertheless imposed a rejection under 35 U.S.C. §103 over the references to Hogan and the reference to Goldsborough on the grounds that the claims are broader than the embodiment which the Examiner accepts provides an unexpected result. The applicant does not believe the present claims are broader than the conditions demonstrated to achieve the unexpected result, and hence the applicant asserts that the rejection should be reconsidered and withdrawn.

First, the Examiner states that it is agreed that the specific condition of adding “basic FGF to Knockout D-MEM media” defines the specific condition. The applicant has previously demonstrated that the use of basic FGF, as opposed to other FGFs is not critical to the unexpected effect. The data provided by the Ludwig declaration submitted herewith is intended to establish that the effect cannot be due to anything in the serum replacement, other than the factors recited in the claims of this patent application. The Examiner previously argued that there was insufficient information in the specification to determine if these factors were sufficient. It is asserted by the applicant that the specification predicts the recited factors would be sufficient. The data presented in the Ludwig declaration presented here establishes that this prediction is, in fact, correct.

Thus the applicant asserts that the claims of this applicant are not made obvious by the prior art combination of references. As before, the applicant asserts that the sufficiency of FGF, when combined with the elements of a serum replacement recited in the claims, to culture stem cells is not predicted in the prior art. The applicant has earlier demonstrated that there is no particular criticality to the use of basic FGF, as opposed to other FGFs, and the applicant has demonstrated here that there is no particular criticality to the particular serum replacement product. In fact, serum replacements made up from constituents recited in the claims will suffice to produce the unexpected effect. Accordingly, the applicant asserts that the logic of the rejection is no longer applicable, based on the evidence in the record, and that the rejection should be reconsidered and withdrawn.

Reconsideration of the merits of this patent application and its early allowance is respectfully requested.

Respectfully submitted,



Nicholas J. Seay  
Reg. No. 27,386  
Attorney for Applicant  
QUARLES & BRADY LLP  
P O Box 2113  
Madison, WI 53701-2113

TEL 608/251-5000  
FAX 608/251-9166

QBMAD\371297.1